

# A coinfection of severe leptospirosis and scrub typhus in Indian Himalayas

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## ABSTRACT

Scrub typhus and leptospirosis are zoonosis and systemic febrile illnesses with diverse, nonspecific clinical manifestations, and shared risk factors for coinfection. Diagnosis of the coinfection is dependent on laboratory serological tests, which are under used. A coinfection from Uttarakhand Himalayan region is not yet reported. A 25-year-old man from altitude of 2126 feet above sea level presented with fever, myalgia, jaundice, oliguria, mental confusion, and tender hepatomegaly. Investigations revealed leukocytosis, thrombocytopenia, impaired liver function tests, renal dysfunction with neurological involvement. *Leptospira* immunoglobulin IgM enzyme linked immunosorbent assay (ELISA) and scrub typhus immunochromatography test were positive. This coinfection is first to be documented in this holy Indian Himalayas. Clinical suspicion, early laboratory diagnosis, and early treatment could prevent complications and fatal outcomes. Coinfection of this type may be considered when there is persistence of fever and a treatment response to doxycycline.

**Keywords:** Acute febrile illness, primary care, rickettsiosis, serology, spirochaetosis, zoonosis

## Introduction

Scrub typhus, a rickettsial zoonosis, is caused by *Orientia tsutsugamushi* and transmitted by bites of infected chiggers (larval mites). Leptospirosis, a spirochetal zoonosis, is caused by pathogenic strains of *Leptospira interrogans* and transmitted by indirect/direct contact with water, soil, or urine of infected animals.<sup>[1]</sup> Both these diseases are widespread in tropical and subtropical regions with shared risk patterns like outdoor activities of host, rodent as a reservoir, and common seasonal spread.<sup>[2]</sup>

The clinical features associated are often nonspecific and varied. Hence, a coinfection with two uncommon diseases is often underdiagnosed.<sup>[3]</sup> A high index of suspicion by primary physicians is needed in patients of endemic regions presenting

with acute febrile illness (AFI), myalgia, headache, rash, pulmonary involvement, hepatosplenomegaly, leukocytosis, and thrombocytopenia which may be suggestive of a coinfection with scrub typhus and leptospirosis considering the high mortality rate (up to 30%).<sup>[4]</sup> Even though both diseases are endemic and seasonally prevalent in India, they are less commonly reported from Uttarakhand Himalayan region (prevalence of 11.2% for scrub typhus and 0.3% for leptospirosis respectively, presumably due to poor suspicion and lack of laboratory facilities in the hilly region.<sup>[5,6]</sup> And coinfection from this region is yet to be reported.

Thereby, we report a case from the Indian Himalayan region of coinfection with scrub typhus and severe leptospirosis.

## Case Report

A 25-year-old postgraduate man, from high altitude (2126 feet above sea level) region of Uttarakhand, Himalayas, presented to the emergency in September (post monsoon season) with 15 days history of intermittent low--moderate grade fever (without diurnal variations), chills, malaise, and myalgia. He developed

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bilious nonprojectile vomiting, mild persistent diarrhea, and jaundice with associated decreased appetite for 5 days. Jaundice was associated with dark colored urine and one episode of dark colored stool with no pruritus. He also had decreased urine output for 4 days. His mental status has deteriorated over last 2 days. There was no history of headache, seizure, rash, conjunctival suffusion, abdominal pain, cough, or breathlessness. No significant treatment history. His past and personal history was insignificant. There was no history of recent travel, exposure to bite/animal contacts, blood transfusion, or any high risk sexual behavior. He was a nonsmoker and nonalcoholic. However, his area of living was in the hilly endemic zone infested with ticks, mites, insects, and rodents.

On examination patient was drowsy (GCS-E3V4M6) and icteric with normal vitals except blood pressure of 90/50 mmHg at emergency room. Per abdomen examination revealed tender hepatomegaly, palpable just below the right costal margin. Other systemic examination was unremarkable including no signs of meningism.

Patient was provisionally diagnosed as a case of acute/subacute undifferentiated febrile illness with multiorgan dysfunction syndrome and was started on broad spectrum antibiotics (meropenem, linezolid, and levofloxacin) in view of acute liver failure after sending routine investigations and fever workup including blood culture. His reports showed white blood cell count of 27,000/mm<sup>3</sup> (N81L9M4), platelet count of 80,000/mm<sup>3</sup>, total bilirubin of 30 mg/dl (direct-16 mg/dl), albumin of 2.38 mg/dl, urea of 380 mg/dl, and creatinine of 9.0 mg/d. Ultrasound abdomen showed bilateral grade-1 renal parenchymal disease with gall bladder sludge. Chest X-ray and 2-D echo were normal. Hemodialysis was done in view of metabolic acidosis, uremic encephalopathy, and oliguria. Fever workup came out to be positive for scrub typhus by immunochromatographic test. Later on immunoglobulin IgM ELISA leptospirosis came to be positive. Antibiotics were de-escalated to doxycycline (100 mg BD, 14 days) and later on injection ceftriaxone (1 gm BD, 7 days). Over the course of hospital stay he developed mild type 1 respiratory failure [Table 1] due to possibly pulmonary edema and was started on noninvasive ventilation (NIV) and hemodialysis. Clinical and radiographic resolution was noted and patient was weaned off NIV over 3 days.

Patient improved over the course of hospital stay, symptoms/signs resolved with no further fever spikes. Patient was discharged with final diagnosis of coinfection with severe leptospirosis (Weil syndrome) and scrub typhus.

## Discussion

We hypothesize, our case had presented with symptoms of both diseases, of leptospirosis in form of acute undifferentiated fever, myalgia, severe liver and kidney injuries, and of scrub typhus in form of prolonged fever, thrombocytopenia, and multiorgan dysfunctions. And case responded to doxycycline, ceftriaxone,

**Table 1: Arterial blood gas (ABG) analysis of the patient over hospital stays**

ABG	D2	D3 (postdialysis)	D12 (type 1 respiratory failure)	D13
pH	7.219	7.46	7.5	7.4
PO <sub>2</sub>	120	93.5	50	92
PO <sub>2</sub> /FIO <sub>2</sub>	571	445	180	438
PCO <sub>2</sub>	20	27.5	21	29
HCO <sub>3</sub> <sup>-</sup>	8.0	20.0	18	20
NA <sup>+</sup>	132	137	133	135
K <sup>+</sup>	4.5	4.3	4.8	4.8
Lactate	0.3	0.7	2.5	1.3

and supportive treatments. This coinfection is first to be reported from Himalayas. As primary care physicians are one of the initial points of contact, it is crucial for them to know about the rare associations of common diseases like this case and their right approach.

Leptospirosis and scrub typhus are often neglected tropical diseases bearing similar seasonal pattern and rodent as a common reservoir. Their common epidemiology creates an opportunity of dual infections.<sup>[3]</sup> This coinfection has previously been reported from various endemic regions like Thailand and Taiwan but only four case reports of serological dual infections have been reported from India.<sup>[1-3,7-9]</sup> The incidence of leptospirosis increases after the rainy season (September–November) because of waterlogging resulting in contact with animal's urine similar to scrub typhus that increases due to increase in trombiculid mite populations in growth of scrubs.<sup>[3]</sup> Hence, primary physicians have to keep in mind possibility of these dual infections in rainy seasons.

The clinical manifestations of both diseases can be nonspecific: fever, headache, skin rash, and myalgia. Calf tenderness (57%) and conjunctival suffusion (34%) are more specific for leptospirosis and eschar (57%) for scrub typhus.<sup>[7]</sup> Once immunologic phase sets in, fever is usually absent in leptospirosis and patient may present with organ failures (Weil's syndrome). This is in contrast to scrub typhus where fever continues as major clinical presentation including organ failures as severity increases. In severe cases, both diseases can progress into any organ failure.<sup>[4]</sup> However, the attached table describes percentage wise organ involvements of both with reference to our case [Table 2].

Doxycycline is used for mild leptospirosis, but for life-threatening leptospirosis high-dose penicillin (or ceftriaxone) remains the drug of choice.<sup>[7]</sup> Hence, doxycycline is recommended to treat patients with this coinfection and is life-saving in regions with high endemicity.<sup>[1]</sup> It is better to start the antimicrobials covering both the spectrum and de-escalating later on. We followed the same protocol in our case and the patient responded well. Hence, first contact physicians can use both drugs in a case of AFI with prolonged fever, thrombocytopenia, multiorgan dysfunctions.

**Table 2: Indian studies on leptospira and scrub typhus coinfection with a comparative analysis with the current study**

Organ involvement	Mahaj et al. 2012 <sup>[9]</sup>	Diwan et al. 2014 <sup>[8]</sup>	Biswajyoti et al. 2016 <sup>[1]</sup>	Gupta et al. 2016 <sup>[2]</sup>	Present case, 2019
Animal contact/endemic region	Present	Present	Present	Present	Present
Fever	Present	Present	100%	100%	Present
Myalgia/arthritis	Present	Present	16%	50%	Present
Icterus	-	-	-	20%	Present
Eschar	Absent	-	7%	30%	Absent
Maculopapular rash	Present	-	28%	40%	Absent
Lymphadenopathy	Present	-	-	20%	Absent
Conjunctival suffusion	Absent	-	13%	10%	Absent
Calf tenderness	Present	-	-	-	Absent
Hepatomegaly	Absent	Present	41%	50%	Present
Splenomegaly	Present	-	22%	20%	Absent
Oliguria	-	-	9%	-	Present
Lymphocytosis	-	-	-	60%	Present
Thrombocytopenia	Present	Present	-	40%	Present
Hyperbilirubinemia	-	-	-	-	Present
AKI	-	Present	-	40%	Present
Pulmonary involvement	-	Present	-	60%	Present
Neurological involvement	-	Present	-	30%	Present
Cardiological involvement	-	-	-	10%	Absent

The possibility of cross reactivity has been a major issue with ELISA. However, if the clinical features are pointing toward both diseases like our case, sending the samples for testing of both diseases makes a good sense.

### Conclusion

Present report will be beneficial for initiating detailed surveillance of underdiagnosed coinfection of leptospira and scrub typhus by increasing medical awareness in Himalayas. Coinfection of this type may be considered when there is persistence of fever after febrile phase of suspected leptospirosis and response to doxycycline in severe leptospirosis. Early serological diagnosis is important because of excellent response to treatment and timely antimicrobial therapy may prevent complications along with avoidance of antimicrobial resistance in the community.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflict of interest

There is no conflict of interest.

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